UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/787,461 | 03/02/2001 | Esteban Cvitkovich | 13566.105002 | 9636 |

65989 7590 02/27/2007

KING & SPALDING
1185 AVENUE OF THE AMERICAS
NEW YORK, NY 10036-4003

| EXAMINER | |
|---|---|
| SPIVACK, PHYLLIS G | |
| ART UNIT | PAPER NUMBER |
| 1614 | |

| SHORTENED STATUTORY PERIOD OF RESPONSE | MAIL DATE | DELIVERY MODE |
|---|---|---|
| 3 MONTHS | 02/27/2007 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/787,461 | CVITKOVICH ET AL. | |
| | Examiner | Art Unit | |
| | Phyllis G. Spivack | 1614 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *07 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *12-17 and 24-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12-17, 24-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 12-7-6;2-7-07.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicants' Request for Continued Examination (RCE) filed February 7, 2007 is acknowledged and accepted. An Amendment filed December 7, 2006 is further acknowledged. New claims 24-35 are presented. Claims 18-23 are canceled. Accordingly, claims 12-17 and 24-35 are now under consideration.

Information Disclosure Statements filed December 7, 2006 and February 7, 2007, as well as a listing of related cases are acknowledged. Applicants may consider listing the PGPubs on a PTO-1449 form. The related applications have been reviewed.

Applicants have claimed benefit of prior-filed, non-US patent applications:

GB 9911183.3, filed on 13 May 1999

GB 9911346.6, filed 14 May 1999

GB 9927005.0, filed 15 November 1999

GB 9918534.0, filed 5 August 1999

GB 9927106.6, filed 16 November 1999

GB 0007637.2, filed 29 March 2000, and

PCT/GB00/01857, a PCT patent application filed at the United Kingdom Patent Office on Monday, May 15, 2000, claiming priority from the six UK patent applications.

The present application must be an application for a patent for an invention that is also disclosed in the prior applications. The disclosure of the invention in the parent applications and in the later-filed applications must be sufficient to comply with the first paragraph of 35 U.S.C. 112.

The present amendment to claim 12 adds the limitation "at a dose level of about 500 to about 1650 micrograms/$m^2$ body surface area" which finds support in the specification on page 13 and in PCT/GB00/01857 on page 13. However, no clear support for the newly inserted dosage range is found in the prior-filed, non-US patent applications.

As such, the earliest effective U.S. filing date afforded the instant claims is May 15, 2000. Because the instant claims are not entitled to the filing date of any of the GB documents, additional prior art rejections are warranted. The prior acknowledgement of a claim for priority to these documents is withdrawn.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 12-17 and 24-35 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-17 of

copending Application No. 10/492320. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the co-pending application are drawn to the administration of ET-743 for the treatment of various types of tumors that are presently claimed.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 12-17 and 24-35 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims of copending Application No. 10/579251. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims 1-17 of the co-pending application are drawn to the administration of ET-743 for the treatment of various types of tumors that are presently claimed. The open language of the present claims allows for the administration of any number of additional agents.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 12-17 and 24-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

The recitation in claim 12 "at a dose level of about 500 to about 1650 micrograms/m2 body surface area" is vague and indefinite. The recitation finds no support in the specification. The metes and bounds of the term "about" cannot be precisely determined and should be deleted.

Applicants' arguments with respect to claims 12-22 that were previously rejected under 35 U.S.C. 103 as being unpatentable over Taamma et al., Eur. J. Cancer, in view of Barrerra et al., Proceedings of the American Association for Cancer Research, have been considered but are moot in view of the new ground of rejection.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 12-17 and 24-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over both Taamma et al., Eur. J. Cancer, and Cvitkovic et al., ASCO Meeting held May 17, 1999, Abstract published in Clinical Cancer Research and on-line at www. asco.org., in view of Goodman & Gilman.

Taamma teaches cyclic intravenous administration of Et-743 in the treatment of various solid tumors, such as breast or ovarian cancer, for an infusion time of 24 hours every 3 weeks. The patient population included those who were designated "refractory" to standard chemotherapy, and thus these patients, as required by claim 32, had previously been treated for cancer with chemotherapy. Cvitkovic teaches a dosage range of 50-1800 $mg/m^2$ to be administered as an infusion over 24 hours every 3 weeks. The number of cycles taught is 1-8 with 2 being the median number. As required by claim 30, Cvitkovic includes such tumor types as colorectal, sarcoma, breast, ovary, renal, bladder, gastric, ACUP, larynx, melanoma and osteosarcoma. As required by claims 31 and 32, one partial response was seen in a patient with

metastatic breast cancer refractory to anthracycline and docetaxel, and another partial response was observed in a heavily pretreated patient with metastatic osteosarcoma. As required by claims 16 and 28, a period of recovery between doses to be administered in cycles is conventional practice in the treatment of tumors. As required by claims 34 and 35, see the Tables on page 930 in Goodman & Gilman, where dexamethasone is shown to be effective as an antiemetic in cancer chemotherapeutic regimens.

In view of the teachings of Taamma and Cvitkovic, one skilled in the oncology art would have been motivated to seek an optimal dosing regimen for ET-743 with respect to dosages, infusion times and intervals of administration through no more than routine experimentation. It is clear from the prior art that the determination of an optimal dosing regimen depends on tumor type, the stage at which a diagnosis is made, the presence or absence of metastasis, prior therapy, the over-all condition of the patient and the avoidance of adverse drug effects, such as thrombopenia, neutropenia, acute renal failure and transaminitis. Ample motivation to treat a human patient for cancer is provided for administering ET-743, optionally in combination with an additional drug, such as an antiemetic, with a reasonable expectation of success. Such determinations are within the purview of those skilled in the oncology art through no more than routine experimentation.

No claim is allowed.

Jimeno et al., ASCO Meeting held May 17, 1999, Abstract published in Clinical Cancer Research and on-line at www. asco.org, is cited to show further the state of the

art. Twelves et al., Clinical Cancer Research, teaches the administration of 1650 mcg/$m^2$ of ET-743 through IV infusion for 24 hours every 3 weeks for good risk patients.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Phyllis G. Spivack whose telephone number is 571-272-0585. The Examiner can normally be reached from 10:30 to 7 PM.

If attempts to reach the Examiner by telephone are unsuccessful after one business day, the Examiner's supervisor, Ardin Marschel, can be reached 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Phyllis Spivack

February 14, 2007

Phyllis Spivack

1614

PHYLLIS SPIVACK
PRIMARY EXAMINER